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=> s g protein coupled receptor or gpcr
L1       86755 G PROTEIN COUPLED RECEPTOR OR GPCR

=> sl1 and gpcr39 or gpr39
L2         204 SL1 AND GPCR39 OR GPR39

=> s l2 and (ionizable metal or nickel or copper cadmium)
L3           0 L2 AND (IONIZABLE METAL OR NICKEL OR COPPER CADMIUM)

=> s l2 and (ionizable metal or nickel or copper or  cadmium)
L4           1 L2 AND (IONIZABLE METAL OR NICKEL OR COPPER OR CADMIUM)

=> d ibib abs l4

L4   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:        2005:1020555  CAPLUS <<LOGINID::20080428>>
DOCUMENT NUMBER:         143:320266
TITLE:                   Genes with differential expression profile
between
                         human dental pulp stem cells and mesenchymal
stem
                         cells and use for regenerating tooth germ
INVENTOR(S):             Ueda, Minoru; Yamada, Yoichi
PATENT ASSIGNEE(S):      Hitachi Medical Corp., Japan
SOURCE:                  Jpn. Kokai Tokkyo Koho, 246 pp.
                         CODEN: JKXXAF
DOCUMENT TYPE:           Patent
LANGUAGE:                Japanese
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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     JP 2005253442        A     20050922    JP 2004-111582
20040309
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PRIORITY APPLN. INFO.: JP 2004-111582
20040309
AB The present invention relates to a group of genes whose expression profile
are different between human dental pulp stem cells and mesenchymal stem
cells, as well as a method for regenerating tooth germ using these genes.
According to the present invention, the gene expression profiles and
cluster anal. between human dental pulp stem cells (hDPSCs) and
mesenchymal stem cells (hMSCs) as representative populations of
odontoprogenitor and osteoprogenitor cell were revealed, and a group of
genes whose expression profile are different between human dental pulp
stem cells and mesenchymal stem cells was identified. By utilizing the
groups of the genes of the present invention together with the dental pulp
stem cells and mesenchymal stem cells, hard tissue such as tooth germ,
dental pulp, dentin or bone can be regenerated. The present inventors
investigated the gene expression profiles and cluster anal. between human
dental pulp stem cells (hDPSCs) and mesenchymal stem cells (hMSCs) as
representative populations of odontoprogenitor and osteoprogenitor cells,
resp. At first, the present inventors confirmed the differential
expression of Alk. phosphatase (ALP) activity, Dentin matrix protein 1
(DMP 1), Dentin phosphosialoprotein (DSPP) using by real time
reverse-transcriptase polymerase chain reaction (RT-PCR) in total RNA from
primary cultures. The no. of genes in hDPSCs(I) that were up-regulated by
2>-fold, compared to hMSCs, was 614 (Table, IV). On the other band, the
no. of genes down regulated by <2-fold in hDPSCs (I) was 296 (Table III,
IV).

=> l2 and (agonist# or antagonist#)
L5 42 L2 AND (AGONIST# OR ANTAGONIST#)

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6 22 DUP REM L5 (20 DUPLICATES REMOVED)

=> d ibib abs l6 1-22

L6 ANSWER 1 OF 22 SCISEARCH COPYRIGHT (c) 2008 The Thomson Corporation on
STN
ACCESSION NUMBER: 2008:483049 SCISEARCH <<LOGINID::20080428>>
THE GENUINE ARTICLE: 282UC
TITLE: Obestatin promotes survival of pancreatic beta-

cells and
human islets and induces expression of genes involved in
the regulation of beta-cell mass and function
AUTHOR: Granata, Riccarda (Reprint); Settanni, Fabio; Gallo,
Davide; Trovato, Letizia; Biancone, Luigi; Cantaluppi,
Vincenzo; Nano, Rita; Annunziata, Marta; Campiglia,
Pietro; Arnoletti, Elisa; Ghe, Corrado; Volante, Marco;
Papotti, Mauro; Muccioli, Giampiero; Ghigo, Ezio
CORPORATE SOURCE: Univ Turin, Dept Internal Med, Div Endocrinol & Metab, Lab
Mol & Cellular Endocrinol, Corso Dogliotti 14, I-10126
Turin, Italy (Reprint); Univ Turin, Dept Internal Med, Div
Endocrinol & Metab, Lab Mol & Cellular Endocrinol, I-10126
Turin, Italy; Univ Turin, Dept Internal Med, Div
Endocrinol & Metab, Turin, Italy; Univ Vita Salute San
Raffaele, San Raffaele Sci Inst, Transplant Unit, Dept
Med, Milan, Italy; Univ Salerno, Dept Pharmaceut Sci,
I-84100 Salerno, Italy; Univ Turin, Dept Anat Pharmacol &
Forens Med, Turin, Italy; Univ Turin, San Luigi Hosp,
Turin, Italy; Univ Turin, Dept Clin & Biol Sci, Turin,
Italy
riccarda.granata@unito.it
COUNTRY OF AUTHOR: Italy
SOURCE: DIABETES, (APR 2008) Vol. 57, No. 4, pp. 967-979.
ISSN: 0012-1797.
PUBLISHER: AMER DIABETES ASSOC, 1701 N BEAUREGARD ST, ALEXANDRIA, VA
22311-1717 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 50
ENTRY DATE: Entered STN: 17 Apr 2008
Last Updated on STN: 17 Apr 2008

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB OBJECTIVE - Obestatin is a newly discovered peptide encoded by the ghrelin gene whose biological functions are poorly understood. We investigated obestatin effect on survival of beta-cells and human pancreatic islets and the underlying signaling pathways.

RESEARCH DESIGN AND METHODS - beta-Cells and human islets were used to assess obestatin effect on cell proliferation, survival, apoptosis, intracellular signaling, and gene expression.

RESULTS - Obestatin showed specific binding on HIT-T15 and INS-1E beta-cells, bound to glucagon-like peptide-1 receptor (GLP-1R), and

recognized ghrelin binding sites. Obestatin exerted proliferative, survival, and antiapoptotic effects under serum-deprived conditions and interferon-gamma/tumor necrosis factor-alpha/interleukin-1 beta treatment, particularly at pharmacological concentrations. Ghrelin receptor ***antagonist*** [D-Lys(3)]-growth hormone releasing peptide-6 and anti-ghrelin antibody prevented obestatin-induced survival in beta-cells and human islets. beta-Cells and islet cells released obestatin, and addition of anti-obestatin antibody reduced their viability. Obestatin increased beta-cell cAMP and activated extracellular signal-related kinase 1/2 (ERK1/2) and phosphatidylinositol 3-kinase (PI 3-kinase)/Akt,; its antiapoptotic effect was blocked by inhibition of adenylyl cyclase/cAMP/protein kinase A (PKA), PI 3-kinase/Akt, and ERK1/2 signaling. Moreover, obestatin upregulated GLP-1R mRNA and insulin receptor substrate-2 (IRS-2) expression and phosphorylation. The GLP-1R ***antagonist*** exendin-(9-39) reduced obestatin effect on beta-cell survival. In human islets, obestatin, whose immunoreactivity colocalized with that of ghrelin, promoted cell survival and blocked cytokine-induced apoptosis through cAMP increase and involvement of adenylyl cyclase/cAMP/PKA signaling. Moreover, obestatin 1) induced Pl 3-kinase/Akt, ERK1/2, and also cAMP response element-binding protein phosphorylation; 2) stimulated insulin secretion and gene expression; and 3) upregulated GLP-1R, IRS-2, pancreatic and duodenal homeobox-1, and glucokinase mRNA.

CONCLUSIONS - These results indicate that obestatin promotes beta-cell and human islet cell survival and stimulates the expression of main regulatory beta-cell genes, identifying a new role for this peptide within the endocrine pancreas.

L6 ANSWER 2 OF 22 WPIDS COPYRIGHT 2008 THE THOMSON CORP on STN
DUPLICATE 1
ACCESSION NUMBER: 2008-C47219 [18] WPIDS
DOC. NO. CPI: C2008-075334 [18]
TITLE: Identifying compounds that enhance glucose control and are effective for preventing or treating pathologies related with an impaired carbohydrate metabolism, e.g. diabetes, by using G protein coupled receptor 39 (***GPR39***) protein
DERWENT CLASS: B04; D16
INVENTOR: MOECHARS D W E; MOREAUX B C J; VER DONCK L A L
PATENT ASSIGNEE: (JANC-C) JANSSEN PHARM NV

COUNTRY COUNT: 119

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2007141322	A1	20071213	(200818)*	EN	75[6]	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2007141322	A1	WO 2007-EP55636	20070608

PRIORITY APPLN. INFO: EP 2006-115158 20060608

AN 2008-C47219 [18] WPIDS

AB WO 2007141322 A1 UPAB: 20080313

NOVELTY - Identifying compounds that enhance glucose control in a subject and which are effective for preventing and/or treating pathologies related with an impaired carbohydrate metabolism, in particular in the prevention and/or treatment of diabetes including its associated complications, or of the metabolic syndrome including its associated complications, comprises the use of all or part of the ***GPR39*** protein.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are:

(1) a method for identifying a compound that enhances glucose regulation in a subject and which are effective for preventing and/or treating pathologies related with an impaired carbohydrate metabolism, in particular in the prevention and/or treatment of diabetes including its associated complications, or of the metabolic syndrome including its associated complications;

(2) a method to identify compounds that modulate carbohydrate metabolism;

(3) use of an isolated nucleic acid sequence selected from: (a) a nucleic acid sequence encoding all or part of the polypeptides of SEQ ID NO. 2 or 4; (b) a nucleic acid sequence comprising SEQ ID NO. 1 or 3; or (c) a nucleic acid sequence having at least 80% sequence identity to SEQ ID NO. 1 or 3, for the method above;

(4) use a vector comprising the nucleic acid sequence, for the method above;

(5) use of a host cell comprising the nucleic acid sequence or vector, for the method above;

(6) a pharmaceutical composition for the treatment of impaired

glucose control in a human or animal comprising a ***GPR39*** receptor
agonist or ***antagonist*** ;
(7) use of a ***GPR39*** ***agonist*** or
antagonist in the manufacture of a medicament for the treatment of
a disease condition related to an impaired carbohydrate metabolism, in
particular diabetes (including associated complications), including Type 1
(insulin-dependent or IDDM), Type 2 (non-insulin-dependent diabetes
mellitus), maturity-onset diabetes of the young (MODY), and gestational
diabetes;
(8) a diagnostic product comprising an isolated nucleic acid
sequence selected from: (a) a nucleic acid sequence encoding all or part
of the polypeptides of SEQ ID NO. 2 or 4; (b) a nucleic acid sequence
comprising SEQ ID NO. 1 or 3; or (c) a nucleic acid sequence having at
least 80% sequence identity to SEQ ID NO. 1 or 3; and
(9) a diagnostic product comprising all or part of the
GPR39 receptor protein.
ACTIVITY - Antidiabetic. No biological data given.
MECHANISM OF ACTION - ***GPR39*** - ***Agonist*** ;
GPR39 - ***Antagonist*** .
USE - The methods, isolated nucleic acid sequence, vector, and host
cell are useful for identifying compounds that enhance glucose control in
a subject and which are effective for preventing and/or treating
pathologies related with an impaired carbohydrate metabolism, in
particular in the prevention and/or treatment of diabetes including its
associated complications, or of the metabolic syndrome including its
associated complications. The ***GPR39*** ***agonist*** or
antagonist is useful in the manufacture of a medicament for the
treatment of a disease condition related to an impaired carbohydrate
metabolism, in particular diabetes (including associated complications),
including Type 1 (insulin-dependent or IDDM), Type 2 (non-insulin-
dependent diabetes mellitus), maturity-onset diabetes of the young (MODY),
and gestational diabetes (all claimed).

L6 ANSWER 3 OF 22 WPIDS COPYRIGHT 2008 THE THOMSON CORP on STN
DUPLICATE 2
ACCESSION NUMBER: 2007-373447 [35] WPIDS
DOC. NO. CPI: C2007-135335 [35]
TITLE: Use of the triazole compound in the manufacture of a
medicament for the treatment or prophylaxis of e.g. acute
fatigue syndrome, adipogenesis, adiposity, Alzheimer's
disease, anorexia

DERWENT CLASS: B02; B03; C02
INVENTOR: BOEGLIN D; DEMANGE L; FEHRENTZ J; MARTINEZ J; MOULIN A;
PERRISSOUD D
PATENT ASSIGNEE: (CNRS-C) CENT NAT RECH SCI; (UYMO-N) UNIV MONTPELLER I;
(UYMO-N) UNIV MONTPELLER II; (UYMO-N) UNIV MONTPELLIER I;
(UYMO-N) UNIV MONTPELLIER II; (ZENT-N) ZENTARIS GMBH
COUNTRY COUNT: 115

PATENT INFO ABBR.:

PATENT NO	KIND DATE	WEEK	LA	PG	MAIN IPC
WO 2007020013	A2 20070222	(200735)*	EN	255[46]	
EP 1757290	A1 20070228	(200735)	EN		
US 20070037857	A1 20070215	(200737)	EN	123[46]	
US 20070208061	A2 20070906	(200760)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2007020013	A2	WO 2006-EP7945	20060811
US 20070037857	A1 Provisional	US 2005-707941P	20050815
EP 1757290	A1	EP 2005-17732	20050816
US 20070037857	A1 Provisional	US 2005-708543P	20050816
US 20070037857	A1	US 2006-502473	20060811
US 20070208061	A2 Provisional	US 2005-707941P	20050815
US 20070208061	A2 Provisional	US 2006-787543P	20060331
US 20070208061	A2	US 2006-502473	20060811

PRIORITY APPLN. INFO: US 2006-787543P 20060331
US 2005-707941P 20050815
EP 2005-17732 20050816

AN 2007-373447 [35] WPIDS
AB WO 2007020013 A2 UPAB: 20070604
NOVELTY - In the manufacture of a medicament for the treatment or prophylaxis of conditions in mammals that are mediated by Growth hormone secretagogue (GHS) receptors, a triazole compound is used.
DETAILED DESCRIPTION - In the manufacture of a medicament for the treatment or prophylaxis of physiological and/or pathophysiological conditions in mammals that are mediated by GHS receptors, a triazole compound of formula (I) is used.
R1,R2=(cyclo)alkyl, cycloalkylalkyl, (hetero)aryl, (hetero)arylalkyl, heterocyclyl, heterocyclylalkyl (all optionally mono- - tri-substituted by G), H, alkenyl, alkynyl, (aryl)alkylsulfonyl or arylsulfonyl (preferably (aryl)alkyl, (hetero)aryl or heteroarylalkyl (all optionally mono- - tri-substituted by G));
G=halo, N3, CN, NR7R8, OH, NO2, (aryl)alkyl, aryl, O-(aryl)alkyl or O-aryl;
R3,R4=H or E;

E=alkyl, (hetero)aryl, heterocyclyl, Q1, (aryl)
alkylsulfonyl,
arylsulfonyl, alkyl-S-alkyl or alkyl-S-H (all are optionally mono -
-tri-substituted in the (hetero)aryl, (hetero)arylalkyl,
heterocyclyl
and/or heterocyclylalkyl group by G) (preferably Q1 optionally mono
-
-tri-substituted in the (hetero)aryl, (hetero)arylalkyl,
heterocyclyl and
heterocyclylalkyl group by G);
Q1=(hetero)arylalkyl, heterocyclylalkyl, alkyl-O-(hetero)
aryl,
alkyl-O-(hetero)arylalkyl, alkyl-O-heterocyclyl, alkyl-O-
heterocyclylalkyl, alkyl-CO-(hetero)aryl, alkyl-CO-(hetero)
arylalkyl,
alkyl-CO-heterocyclyl, alkyl-CO-heterocyclylalkyl, alkyl-C(O)O-
(hetero)aryl, alkyl-C(O)O-(hetero)arylalkyl, alkyl-C(O)O-
heterocyclyl,
alkyl-C(O)O- heterocyclylalkyl, alkyl-CO-NH2, alkyl-CO-OH, alkyl-
NH2 or
alkyl-NH-C(NH)-NH2;
R5=H, (cyclo)alkyl, cycloalkylalkyl, (hetero)aryl,
(hetero)arylalkyl, heterocyclyl, heterocyclylalkyl, CO-(aryl)alkyl,
CO-cycloalkyl, CO-cycloalkylalkyl, CO-(hetero)aryl, CO-
heteroarylalkyl,
CO-heterocyclyl, CO-heterocyclylalkyl, - CO-Casterisk(R9R10)-NH2,
CO-CH2-Casterisk(R9R10)-NH2, CO-Casterisk(R9R10)-CH2-NH2,
(aryl)alkylsulfonyl, arylsulfonyl (all optionally mono- - tri-
substituted
by G) (preferably H, CO-(cyclo)alkyl, CO-(hetero)aryl,
CO-(hetero)arylalkyl, CO-heterocyclyl, CO-Casterisk(R9R10)-NH2,
CO-CH2-Casterisk(R9R10)-NH2, -CO-Casterisk(R9R10)-CH2NH2
(optionally mono-
- tri-substituted by G);
R6-R8=H, (cyclo)alkyl or cycloalkylalkyl (preferably H);
R9,R10=H, alkyl, natural alpha-amino acid side chain or
unnatural
alpha-amino acid side chain (preferably H or alkyl);
m=0 - 2 (preferably 0).
The asterisk indicates a carbon atom of R or S configuration
when
chiral. INDEPENDENT CLAIMS are included for the following:
(1) new 190 triazole compounds (B1) e.g. (R)-N-(1-(5-(2-(1H-
indol-3-
yl)ethyl)-4-(2,4-dimethoxybenzyl)-4H-1,2,4-triazol-3-yl)-2-(1H-
indol-3-
yl)ethyl)-2-amino-2-methylpropanamide;
(2) a pharmaceutical composition comprising compound (B1).
ACTIVITY - Muscular-Gen.; Immunomodulator; Nootropic;
Neuroprotective; Anabolic; Eating-Disorders-Gen.; Tranquilizer;
Cardiant;
CNS-Gen.; Osteopathic; Antiinflammatory; Gastrointestinal-Gen.;
Antiulcer;
Endocrine-Gen.; Antidepressant; Anorectic; Antidiabetic;
Immunosuppressant; Nephrotropic; Neuroleptic; Hemostatic;
Cytostatic;
Vasotropic; Anti-HIV; Hepatotropic; Respiratory-Gen.; Vulnerary;
Hypnotic.
(R)-N-(1-(4-(4-Methoxybenzyl)-5-phenethyl-4H-1,2,4-triazol-3-yl)-2-
(1H-

indol-3-yl)ethyl)piperidine-4-carboxamide (A) (0.1 micrograms/kg/day by
subcutaneous injection) was tested for treatment of cachexia as given in
Ibanez I et al. (J Endocrinol. 2000, 165(3):537-544). using a cachexia
model system. On day 3, 6, 10, 13, 15 and day 17, the body weight change
(g) was -3.02, 2.95, 11.97, 9.32, -2.78 and -8.27 g for the rats with
adjuvant induced arthritis+vehicle and was -5.32, 2.98, 14.92, 19.08, 7.05
and 1.47 g arthritis+the compound (A).

MECHANISM OF ACTION - GHS receptor ***antagonist*** or ***agonist*** ; GHS receptors modulator. Motilin receptor-ligand (MTL)
binding assay using human recombinant HEK-293 cells were carried out as
given in Feighner SD et al. (Science 1999, 284:2184-2188). to test
(R)-N-(1-(4-(2,4-dimethoxybenzyl)-5-phenethyl-4H-1,2,4-trizol-3-yl)-2-(1H-
indol-3-yl)ethyl)picolinamide. The IC50 value was 1.39 muM against MTL-R
1a receptor.

USE - In the manufacture of a medicament for the treatment or
prophylaxis of physiological and/or pathophysiological conditions (e.g.
acute fatigue syndrome and muscle loss following election surgery,
adipogenesis, adiposity, age-related decline of thymic function,
age-related functional decline (ARFD) in the elderly, aging disorder in
companion animals, Alzheimer's disease, anorexia, anxiety, blood pressure
(lowering), body weight gain/reduction, bone fracture repair, bone
remodeling stimulation, cachexia and protein loss reduction, cardiac
dysfunctions, cartilage growth stimulation, catabolic disorders, catabolic
side effects of glucocorticoids, catabolic state of aging, central nervous
system disorder, chronic dialysis, chronic fatigue syndrome, cognitive
function improvement (e.g. Alzheimer's disease), disctraction
osteogenesis, complications associated with transplantation, congestive
heart failure, Crohn's disease, ulcerative colitis, Cushing's syndrome,
depressions, frailty, gastric postoperative ileus, glycemic control
improvement, growth promotion in livestock, growth retardation associated
with the Prader-Willi syndrome and Turner's syndrome, hip fractures,
hunger, immune deficiency in individuals with a depressed T4/T8 cell
ratio, immune response improvement to vaccination, immune system
stimulation in companion animals, immunosuppression, inflammatory bowel
disease, diabetes, intrauterine growth retardation, lipodystrophy

(e.g.
HIV-induced), metabolic homeostasis maintenance, muscle
mass/strength
increase, muscular atrophy, Noonan's syndrome, obesity,
osteoporosis,
postoperative ileus, psychosocial deprivation, pulmonary
dysfunction,
recovery of burn patients, renal failure, sarcopenia,
schizophrenia,
sensory function maintenance (e.g. hearing, sight, olefaction and
taste),
skeletal dysplasia, skin thickness maintenance, sleep disorders,
thrombocytopenia, tumor cell proliferation, wasting in connection
with
AIDS, chronic liver disease, chronic obstructive pulmonary disease,
multiple sclerosis or secondary to fractures, wound healing in
mammals
(e.g. human, domestic animals, cattle, livestock, pets, cow, sheep,
pig,
goat, horse, pony, donkey, hinny, mule, hare, rabbit, cat, dog,
guinea
pig, hamster, rat, mouse). For wool growth stimulation in sheep
(claimed).
ADVANTAGE - The compounds are GHS receptor modulates e.g.
GHS
receptors e.g. GHS type 1 receptor, GHS-R1a, GHS-R1b, motilin
receptor,
motilin receptor 1a, neurotensin receptor, TRH receptor, GPR38
(FM1),
GPR39 (FM2), GHS-R subtype, GHS binding site, cardiac
GHS-R,
mammary GHS-R; resistant to degradation by enzymes of the
gastro-intestinal tract and display an improved metabolic stability
and
bioavailability.

L6 ANSWER 4 OF 22 WPIDS COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2007-394966 [37] WPIDS
CROSS REFERENCE: 2007-373447
DOC. NO. CPI: C2007-142598 [37]
DOC. NO. NON-CPI: N2007-296329 [37]
TITLE: Treatment/prophylaxis of
physiological/pathophysiological
conditions (e.g. acute fatigue syndrome,
adipogenesis and
adiposity) mediated by growth hormone secretagogue
receptors, comprises administering triazole
compounds
DERWENT CLASS: B02; B03; C02; S03
INVENTOR: BOEGLIN D; DEMANGE L; FEHRENTZ J; MARTINEZ J;
MOULIN A;
PERRISSOUD D
PATENT ASSIGNEE: (CNRS-C) CENT NAT RECH SCI; (UYMO-N) UNIV
MONTPELLIER I;
(UYMO-N) UNIV MONTPELLIER II; (ZENT-N) ZENTARIS
GMBH
COUNTRY COUNT: 1

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 20070037857	A1	20070215	(200737)*	EN	123[46]	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 20070037857	A1 Provisional	US 2005-707941P	20050815
US 20070037857	A1 Provisional	US 2005-708543P	20050816
US 20070037857	A1	US 2006-502473	20060811

PRIORITY APPLN. INFO: EP 2005-17732 20050816

AN 2007-394966 [37] WPIDS

CR 2007-373447

AB US 20070037857 A1 UPAB: 20070612

NOVELTY - Method for the treatment or prophylaxis of at least one physiological and/or pathophysiological condition in a mammal that is mediated by growth hormone secretagogue (GHS) receptors, comprises administering triazole compounds (I).

DETAILED DESCRIPTION - Method for the treatment or prophylaxis of at least one physiological and/or pathophysiological condition in a mammal that is mediated by growth hormone secretagogue (GHS) receptors, comprises administering triazole compounds of formula (I).

R1, R2 = H, alkenyl, alkynyl, (cyclo)alkyl, cycloalkylalkyl, (hetero)aryl, (hetero)arylalkyl, heterocyclyl, heterocyclylalkyl, alkylsulfonyl, arylsulfonyl or arylalkylsulfonyl (all optionally substituted by up to 3 substituents of halo, F, Cl, Br, I, N3, CN, NR7R8, OH, NO2, alkyl, aryl, arylalkyl, O-alkyl, O-aryl or O-arylalkyl);

R3, R4 = (hetero)aryl, (hetero)arylalkyl, heterocyclyl, heterocyclylalkyl (by up to 3 substituents of halo, F, Cl, Br, I, N3, CN, NR7R8, OH, NO2, alkyl, aryl, arylalkyl, O-alkyl, O-aryl or O-arylalkyl), H, alkyl, alkyl-O-aryl, alkyl-O-arylalkyl, alkyl-O-heteroaryl, alkyl-O-heteroarylalkyl, alkyl-O-heterocyclyl, alkyl-O-heterocyclylalkyl, alkyl-CO-aryl, alkyl-CO-arylalkyl, alkyl-CO-heteroaryl, alkyl-CO-heteroarylalkyl, alkyl-CO-heterocyclyl, alkyl-CO-heterocyclylalkyl, alkyl-C(O)O-aryl, alkyl-C(O)O-arylalkyl, alkyl-C(O)O-heteroaryl, alkyl-C(O)O-heteroarylalkyl, alkyl-C(O)O-heterocyclyl, alkyl-C(O)O-heterocyclylalkyl, alkyl-CO-NH2, alkyl-CO-OH, alkyl-NH2, alkyl-NH-C(N H)-NH2, alkylsulfonyl, arylsulfonyl, arylalkylsulfonyl, alkyl-S-alkyl or alkyl-S-H;

R5 = H, (cyclo)alkyl, cycloalkylalkyl, (hetero)aryl, (hetero)arylalkyl, heterocyclyl, heterocyclylalkyl, CO-alkyl, CO-cycloalkyl, CO-cycloalkylalkyl, CO-aryl, CO-arylalkyl, CO-heteroaryl, CO-heteroarylalkyl, CO-heterocyclyl, CO-heterocyclylalkyl, CO-C(asterisk)(R9R10)-NH2, CO-CH2-C(asterisk)(R9R10)-NH2, CO-C(asterisk)(R9R10)-CH2-NH2, alkylsulfonyl, arylsulfonyl, arylalkylsulfonyl (all optionally substituted by up to 3 substituents of halo, F, Cl, Br, I, N3, CN, NR7R8, OH, NO2, alkyl, aryl, arylalkyl,

O-alkyl, O-aryl or O-arylalkyl);
R6, R7, R8 = H, (cyclo)alkyl or cycloalkylalkyl;
R9, R10 = H, alkyl or (un)natural alpha-amino acid side chain;
m = 0-2; and
asterisk = R or S configuration C when chiral.
An INDEPENDENT CLAIM is included for a pharmaceutical composition
comprising (I) and carrier and/or excipient.
ACTIVITY - Neuroprotective; Nootropic; Anabolic; Eating-Disorders-Gen.; Tranquilizer; Cardiant; CNS-Gen.; Antiinflammatory; Antiulcer; Gastrointestinal-Gen.; Endocrine-Gen.; Antidepressant; Immunostimulant; Immunosuppressive; Antidiabetic; Anorectic; Osteopathic; Neuroleptic; Hypnotic; Cytostatic; Vulnerary; Immunomodulator; Vasotropic.
MECHANISM OF ACTION - GHS receptor modulator; GHS-R1a receptor modulator. (I) were tested for their GHS-R1a modulatory activity using GHS-R1a receptor-ligand binding assays. The results showed that the median inhibitory concentration of (R)-N-(1-(5-(2-(1H-indol-3-yl)ethyl)-4-(4-methoxybenzyl)-4H-1,2,4-triazol-3-yl)-2-(1H-indol-3-yl)ethyl) piperidine-4-carboxamide was 0.3 nM.
USE - The method is useful for the treatment or prophylaxis of at least one physiological and/or pathophysiological condition in a mammal that is mediated by GHS receptors, where the mammal is e.g. human, domestic animals, pets and cow, and the conditions are e.g. Alzheimer's disease, anorexia, anxiety, blood pressure, cardiac depressant, central nervous system disorders, Crohn's disease and ulcerative colitis, Cushing's syndrome, dementia, depressions, immune system stimulation, immunosuppression, inflammation, diabetes, irritable bowel syndrome, Noonan's syndrome, obesity, osteoporosis, postoperative ileus, schizophrenia, sleep disorders, tumor cell proliferation, ventricular dysfunction or reperfusion events, cachexia, wound/burn healing, regulation of energy balance, regulation of food intake or adipogenesis (claimed).
ADVANTAGE - (I) (strong GHS receptor binder) can be administered at lower doses compared to other less potent binders while still achieving equivalent or even superior desired biological effects. (I) have less or no side effects. (I) have improved metabolic stability and/or an improved bioavailability.

ACCESSION NUMBER: 2007:1300723 CAPLUS <<LOGINID::20080428>>
DOCUMENT NUMBER: 147:539679
TITLE: Alleles and polymorphisms associated with type 2
diabetes mellitus and obesity and their
diagnostic use
INVENTOR(S): Salonen, Jukka T.; Hyppoenen, Jelena; Kaikkonen, Jari;
Pirskanen, Mia; Uimari, Pekka; Aalto, Juha-Matti
PATENT ASSIGNEE(S): Oy Jurilab Ltd., Finland
SOURCE: PCT Int. Appl., 456pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007128884	A1	20071115	WO 2007-FI50266	20070509

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

US 20070292412	A1	20071220	US 2007-798002	20070509
PRIORITY APPLN. INFO.:			US 2006-798706P	P 20060509
			US 2006-798774P	P 20060509
			US 2006-805522P	P 20060622
			US 2006-819015P	P 20060707
			US 2006-827306P	P 20060928
			US 2006-863438P	P 20061030
			US 2006-864681P	P

20061107
AB Genes, SNP markers and haplotypes that are markers of susceptibility or
predisposition to type 2 diabetes and obesity and related medical conditions are disclosed. Methods for diagnosis, prediction of clin.
course and efficacy of treatments for type 2 diabetes, obesity and related
phenotypes using polymorphisms in the risk genes are also disclosed. The
genes, gene products and agents of the invention are also useful for
monitoring the effectiveness of prevention and treatment of type 2 diabetes and related traits. Kits are also provided for the diagnosis,
selecting treatment and assessing prognosis of type 2 diabetes. Novel
methods for prevention and 10 treatment of metabolic diseases such as type
2 diabetes based on the disclosed type 2 diabetes genes, polypeptides and
related pathways are also disclosed.
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:330186 CAPLUS <<LOGINID::20080428>>
DOCUMENT NUMBER: 146:354159
TITLE: Multiplex array useful for assaying protein-protein
interaction
INVENTOR(S): Lee, Kevin J.
PATENT ASSIGNEE(S): Sentigen Bioscience, Inc., USA
SOURCE: PCT Int. Appl., 88pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007032793	A1	20070322	WO 2006-US20810	20060530

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM
EP 1893627 A1 20080305 EP 2006-771518 20060530
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR
PRIORITY APPLN. INFO.: US 2005-685565P P 20050527
WO 2006-US20810 W 20060530

AB The described invention shows how multiple interactions between two proteins of interest can be detd. by observing activation or lack thereof of intracellular proteins, following interaction of ligand and receptor.

Multiplex arrays permit screening of test compds. (e.g., receptors, esp. G protein-coupled receptors) against multiple proteins. A multiplex array comprises: a solid substrate having multiple receptacles each contg. a sample of cells transformed or transfected with (a) a first nucleic acid mol. comprising: (i) a nucleotide sequence encoding a first test protein, (ii) a nucleotide sequence encoding a cleavage site for a protease, and (iii) a nucleotide sequence encoding a protein which activates a reporter gene in the cell; (b) a second nucleic acid mol. comprising: (i) a nucleotide sequence which encodes a second test protein whose interaction with the first test protein in the presence of a test compd. of interest is to be measured and (ii) a nucleotide sequence which encodes a protease specific for the cleavage site, wherein the first test protein differs from other first test proteins in each of the samples and the activity of the reporter gene is used to det. activity of the test proteins. A no. of constructs were prepd. encoding specific G protein-coupled receptors (e.g., human .beta.2 adrenergic receptor) fused through a protease-cleavable linker to the tetracycline controlled transactivator tTA. A second set of constructs were also made encoding .beta. arrestin 2 and the catalytic domain of the tobacco etch virus nuclear inclusion A protease. Plasmids encoding the fusion proteins were transfected

into
cells contg. the .beta.-galactosidase gene under control of a tTA
dependent promoter. Treatment with ***agonist*** increased
levels of
.beta.-galactosidase activity when both sets of fusion proteins
were
expressed. A series of adrenergic receptors was tested with two
agonists and two ***antagonists*** .
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE
FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L6 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:174407 CAPLUS <<LOGINID::20080428>>
DOCUMENT NUMBER: 146:244386
TITLE: Mammalian obestatin receptors, ***GPR39*** ,
or
ligands in screening for agents modulating
obestatin
function or for predisposition to obesity, in
treating
obesity, and in regulating blood pressure and
gut
motility
INVENTOR(S): Hsueh, Aaron J. W.; Zhang, Jian; Luo, Ching-Wei
PATENT ASSIGNEE(S): The Board of Trustees of the Leland Stanford
Junior
University, USA
SOURCE: PCT Int. Appl., 42pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007019410	A2	20070215	WO 2006-US30648	20060803
WO 2007019410	A3	20071115		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA,
CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB,
GD,
GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN,
KP,
KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK,
MN,
MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS,
RU,
SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA,
UG,
US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU,
IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF,
BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW,

GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
US 20070042409 A1 20070222 US 2006-499030 20060804
PRIORITY APPLN. INFO.: US 2005-705796P P 20050805
AB A high affinity obestatin receptor is provided; the orphan receptor ***GPR39*** . The receptor mediates obestatin activities. The obestatin
receptor (***GPR39***) and fragments thereof, particularly sol. fragments thereof, are useful as therapeutic agents capable of inhibiting
the action of obestatin. In addn. to use as a therapeutic agent, ***GPR39*** polypeptides are utilized in screening and research methods
for the detn. of specific analogs, ***agonists*** , ***antagonist***
mimetics and agents that modulate prodn., metab., and disposition of
GPR39 activities. Conditions treatable with ***GPR39*** ***agonists*** or ***antagonists*** include regulation of wt., blood
pressure and heart rate, and gastric emptying.

L6 ANSWER 8 OF 22 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2008014592 EMBASE <<LOGINID::20080428>>
TITLE: Research progress on brain-gut peptide obestatin and ghrelin.
AUTHOR: Tang, Sheng-Qiu; Jiang, Qing-Yan (correspondence); Zhang,
Yong-Liang; Zhu, Xiao-Tong; Shu, Gang; Gao, Ping
CORPORATE SOURCE: College of Animal Science, South China Agricultural University, Guangzhou 510642, Guangdong Province, China.
qyjiang@scau.edu.cn
SOURCE: World Chinese Journal of Digestology, (Nov 2007) Vol. 15,
No. 31, pp. 3324-3331.
Refs: 66
ISSN: 1009-3079 CODEN: SHXZF2
COUNTRY: China
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
LANGUAGE: Chinese
SUMMARY LANGUAGE: English; Chinese
ENTRY DATE: Entered STN: 17 Jan 2008
Last Updated on STN: 17 Jan 2008
AB Obestatin and ghrelin are two important brain-gut peptides that can combine with their receptors and exert important biological functions.
Obestatin is a 76-98 amino acid polypeptide segment of proghrelin that
binds to the orphan G-protein-coupled receptor ***GPR39*** , which can
suppress food intake, inhibit jejunal contraction, and decrease

body-weight gain. Ghrelin is a 24-51 amino acid peptide segment of proghrelin that binds to receptor GHS-R, which can enhance appetite and body weight, promote the release of GH, and affect cardiovascular and immune functions. Obestatin is regarded as on biological ***antagonist*** , or a Yin and Yang activated polypeptide of ghrelin.

L6 ANSWER 9 OF 22 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2007750209 MEDLINE <<LOGINID::20080428>>
DOCUMENT NUMBER: PubMed ID: 17717076
TITLE: Importance of constitutive activity and arrestin-independent mechanisms for intracellular trafficking of the ghrelin receptor.
AUTHOR: Holliday Nicholas D; Holst Birgitte; Rodionova Elena A;
Schwartz Thue W; Cox Helen M
CORPORATE SOURCE: Institute of Cell Signalling, Queen's Medical Centre,
Nottingham NG7 2UH, United Kingdom..
nicholas.holliday@nottingham.ac.uk
SOURCE: Molecular endocrinology (Baltimore, Md.), (2007 Dec) Vol.
21, No. 12, pp. 3100-12. Electronic Publication: 2007-08-23.
Journal code: 8801431. ISSN: 0888-8809.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200802
ENTRY DATE: Entered STN: 20 Dec 2007
Last Updated on STN: 27 Feb 2008
Entered Medline: 26 Feb 2008

AB The ghrelin receptor (GhrelinR) and its related orphan ***GPR39*** each display constitutive signaling, but only GhrelinRs undergo basal internalization. Here we investigate these differences by considering the roles of the C tail receptor domains for constitutive internalization and activity. Furthermore the interaction between phosphorylated receptors and beta-arrestin adaptor proteins has been examined. Replacement of the FLAG-tagged GhrelinR C tail with the equivalent ***GPR39*** domain (GhR-39 chimera) preserved G(q) signaling. However in contrast to the GhrelinR, GhR-39 receptors exhibited no basal and substantially decreased ***agonist*** -induced internalization in transiently transfected HEK293 cells. Internalized GhrelinR and GhR-39 were predominantly localized to recycling compartments, identified with transferrin and the monomeric G

proteins Rab5 and Rab11. Both the inverse ***agonist*** [d-Arg (1),
d-Phe(5), d-Trp(7,9), Leu(11)] substance P and a naturally occurring
mutant GhrelinR (A204E) with eliminated constitutive activity inhibited
basal GhrelinR internalization. Surprisingly, we found that
noninternalizing ***GPR39*** was highly phosphorylated and that basal
and ***agonist*** -induced phosphorylation of the GhR-39 chimera was
elevated compared with GhrelinRs. Moreover, basal GhrelinR endocytosis
occurred without significant phosphorylation, and it was not prevented by
cotransfection of a dominant-negative beta-arrestin1(319-418) fragment or
by expression in beta-arrestin1/2 double-knockout mouse embryonic
fibroblasts. In contrast, ***agonist*** -stimulated GhrelinRs
recruited the clathrin adaptor green fluorescent protein-tagged
beta-arrestin2 to endosomes, coincident with increased receptor
phosphorylation. Thus, GhrelinR internalization to recycling compartments
depends on C-terminal motifs and constitutive activity, but the high
levels of ***GPR39*** phosphorylation, and of the GhR-39 chimera, are
not sufficient to drive endocytosis. In addition, basal GhrelinR
internalization occurs independently of beta-arrestins.

L6 ANSWER 10 OF 22 MEDLINE on STN
ACCESSION NUMBER: 2007000971 MEDLINE <<LOGINID::20080428>>
DOCUMENT NUMBER: PubMed ID: 16931650
TITLE: Obestatin acts in brain to inhibit thirst.
AUTHOR: Samson Willis K; White Meghan M; Price Christopher; Ferguson Alastair V
CORPORATE SOURCE: Department of Pharmacological and Physiological Science,
Saint Louis University, 1402 South Grand Boulevard, St.
Louis, MO 63104, USA.. samsonwk@slu.edu
CONTRACT NUMBER: HL68052 (United States NHLBI)
SOURCE: American journal of physiology. Regulatory, integrative and
comparative physiology, (2007 Jan) Vol. 292, No. 1, pp.
R637-43. Electronic Publication: 2006-08-24.
Journal code: 100901230. ISSN: 0363-6119.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200702
ENTRY DATE: Entered STN: 4 Jan 2007
Last Updated on STN: 9 Feb 2007
Entered Medline: 8 Feb 2007
AB Derived from the same prohormone, obestatin has been reported to exert
effects on food intake that oppose those of ghrelin. The obestatin

receptor ***GPR39*** is present in brain and pituitary gland. Since the gene encoding those two peptides is expressed also in those tissues, we examined further the possible actions of obestatin in vivo and in vitro. Intracerebroventricular administration of obestatin inhibited water drinking in ad libitum-fed and -watered rats, and in food-and water-deprived animals. The effects on water drinking preceded and were more pronounced than any effect on food intake, and did not appear to be the result of altered locomotor/behavioral activity. In addition, obestatin inhibited ANG II-induced water drinking in animals provided free access to water and food. Current-clamp recordings from cultured, subfornical organ neurons revealed significant effects of the peptide on membrane potential, suggesting this as a potential site of action. In pituitary cell cultures, log molar concentrations of obestatin ranging from 1.0 pM to 100 nM failed to alter basal growth hormone (GH) secretion. In addition, 100 nM obestatin failed to interfere with the stimulation of GH secretion by GH-releasing hormone or ghrelin and did not alter the inhibition by somatostatin in vitro. We conclude that obestatin does not act in pituitary gland to regulate GH secretion but may act in brain to alter thirst mechanisms. Importantly, in rats the effects of obestatin on food intake may be secondary to an action of the peptide to inhibit water drinking.

L6 ANSWER 11 OF 22 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2007565926 MEDLINE <<LOGINID::20080428>>
DOCUMENT NUMBER: PubMed ID: 17885920
TITLE: Isolation of Zn2+ as an endogenous ***agonist*** of ***GPR39*** from fetal bovine serum.
AUTHOR: Yasuda Shin-ichiro; Miyazaki Takahiro; Munechika Kouji; Yamashita Masami; Ikeda Yoshitaka; Kamizono Akihito
CORPORATE SOURCE: Pharmaceuticals Research Division, Mitsubishi Pharma Corporation, Yokohama, Japan.. Yasuda.Shinichirou@mm.m-pharma.co.jp
SOURCE: Journal of receptor and signal transduction research, (2007) Vol. 27, No. 4, pp. 235-46. Journal code: 9509432. ISSN: 1079-9893.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200711
ENTRY DATE: Entered STN: 22 Sep 2007
Last Updated on STN: 8 Nov 2007
Entered Medline: 7 Nov 2007

AB We attempted to determine natural ***agonists*** of ***GPR39*** in fetal bovine serum (FBS). FBS was conditioned to extract peptides and fractionated by two types of HPLC. The activity of each fraction was monitored by intracellular calcium mobilization. Then the purified active ingredient was analyzed by inductively coupled plasma mass spectrometry. In this fashion, Zn2+ ion was identified as an ***agonist*** of ***GPR39*** , though no peptidergic molecules were found. The calcium-mobilizing activity of Zn2+ was not abolished by pertussis toxin but was by a phospholipase C (PLC) inhibitor, U73122, indicating that the activity of ***GPR39*** is mediated through the Gqalpha -PLC pathway. In addition, Zn2+ also activated mouse and rat ***GPR39*** , showing that the function of ***GPR39*** as a Zn2+ receptor is conserved across species. This study is the first exploration of ***GPR39*** ***agonists*** in FBS and indicates that ***GPR39*** functions as a Gq-coupled Zn2+-sensing receptor.

L6 ANSWER 12 OF 22 SCISEARCH COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2007:125981 SCISEARCH <<LOGINID::20080428>>
THE GENUINE ARTICLE: 126PX
TITLE: Little or no ability of obestatin to interact with ghrelin or modify motility in the rat gastrointestinal tract
AUTHOR: Bassil, A. K.; Haglund, Y.; Brown, J.; Rudholm, T.; Hellstrom, P. M.; Naslund, E.; Lee, K.; Sanger, G. J. (Reprint)
CORPORATE SOURCE: GlaxoSmithKline Inc, Neurol & Gastrointestinal Ctr Excellence Drug Dis, New Frontiers Sci Pk, 3rd Ave, Harlow CM19 5AW, Essex, England (Reprint); GlaxoSmithKline Inc, Neurol & Gastrointestinal Ctr Excellence Drug Dis, Harlow CM19 5AW, Essex, England; Karolinska Inst, Danderyd Hosp, Dept Clin Sci, Div Surg, Stockholm, Sweden; Univ Solna, Karolinska Hosp, Dept Med, Solna, Sweden; Karolinska Inst, S-10401 Stockholm, Sweden
Gareth.J.Sanger@gsk.com

COUNTRY OF AUTHOR: England; Sweden
SOURCE: BRITISH JOURNAL OF PHARMACOLOGY, (JAN 2007) Vol. 150, No.
1, pp. 58-64.
ISSN: 0007-1188.
PUBLISHER: NATURE PUBLISHING GROUP, MACMILLAN BUILDING, 4 CRINAN ST,
LONDON N1 9XW, ENGLAND.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 22
ENTRY DATE: Entered STN: 8 Feb 2007
Last Updated on STN: 8 Feb 2007
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Background and purpose: Obestatin, encoded by the ghrelin gene may inhibit gastrointestinal (GI) motility. This activity was re-investigated.

Experimental approach: Rat GI motility was studied in vitro (jejunum contractility and cholinergically-mediated contractions of forestomach evoked by electrical field stimulation; EFS) and in vivo (gastric emptying and intestinal myoelectrical activity). Ghrelin receptor function was studied using a GTP gamma S assay and transfected cells.

Key results: Contractions of the jejunum or forestomach were unaffected by obestatin 100 nM or 0.01-1000 nM, respectively (P > 0.05 each; n = 4-18). Obestatin (0.1-1 nM) reduced the ability of ghrelin I mu M to facilitate EFS-evoked contractions of the stomach (increases were 42.7 +/- 7.8% and 21.2 +/- 5.0% in the absence and presence of obestatin 1 nM; P < 0.05; n=12); higher concentrations (10-1000 nM) tended to reduce the response to ghrelin but changes were not statistically significant.

Similar concentrations of obestatin did not significantly reduce a facilitation of contractions caused by the 5-HT4 receptor ***agonist*** prucalopride, although an inhibitory trend occurred at the higher concentrations (increases were 69.3 +/- 14.0% and 42.6 +/- 8.7% in the absence and presence of 1000 nM obestatin; n=10). Obestatin (up to 10 mu M) did not modulate recombinant ghrelin receptor function. Ghrelin increased gastric emptying and reduced MMC cycle time; obestatin (1000 and 30,000 pmol kg(-1) min(-1)) had no effects. Obestatin (2500 pmol kg-1 min(-1), starting 10 min before ghrelin) did not prevent the ability of ghrelin (500 pmol kg(-1) min(-1)) to shorten MMC cycle time.

Conclusions and implications: Obestatin has little ability to modulate rat GI motility.

ACCESSION NUMBER: 2006740461 MEDLINE <<LOGINID::20080428>>
DOCUMENT NUMBER: PubMed ID: 16959833
TITLE: ***GPR39*** signaling is stimulated by zinc ions but not by obestatin.
AUTHOR: Holst Birgitte; Egerod Kristoffer L; Schild Enrico; Vickers Steve P; Cheetham Sharon; Gerlach Lars-Ole; Storjohann Laura; Stidsen Carsten E; Jones Rob; Beck-Sickinger Annette G; Schwartz Thue W
CORPORATE SOURCE: Laboratory for Molecular Pharmacology, The Panum Institute, University of Copenhagen, Blegdamsvej 3, DK-2200 Copenhagen, Denmark.
SOURCE: Endocrinology, (2007 Jan) Vol. 148, No. 1, pp. 13-20. Electronic Publication: 2006-09-07. Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200702
ENTRY DATE: Entered STN: 21 Dec 2006 Last Updated on STN: 14 Feb 2007 Entered Medline: 13 Feb 2007

AB ***GPR39*** is an orphan member of the ghrelin receptor family that recently was suggested to be the receptor for obestatin, a peptide derived from the ghrelin precursor. Here, we compare the effect of obestatin to the effect of Zn(2+) on signal transduction and study the effect of obestatin on food intake. Although Zn(2+) stimulated inositol phosphate turnover, cAMP production, arrestin mobilization, as well as cAMP response element-dependent and serum response element-dependent transcriptional activity in ***GPR39*** -expressing cells as opposed to mock-transfected cells, no reproducible effect was obtained with obestatin in the ***GPR39*** -expressing cells. Moreover, no specific binding of obestatin could be detected in two different types of ***GPR39*** -expressing cells using three different radioiodinated forms of obestatin. By quantitative PCR analysis, ***GPR39*** expression was readily detected in peripheral organs such as duodenum and kidney but not in the pituitary and hypothalamus, i.e. presumed central target organs for obestatin. Obestatin had no significant and reproducible effect on acute food intake in either freely fed or fasted lean mice. It is concluded that ***GPR39*** is probably not the obestatin receptor. In

contrast,
the potency and efficacy of Zn(2+) in respect of activating signaling
indicates that this metal ion could be a physiologically relevant ***agonist*** or modulator of ***GPR39*** .

L6 ANSWER 14 OF 22 WPIDS COPYRIGHT 2008 THE THOMSON CORP on STN
DUPLICATE 6
ACCESSION NUMBER: 2006-814717 [82] WPIDS
DOC. NO. CPI: C2006-257430 [82]
TITLE: Use of mammalian ***GPR39*** protein or its modulator
to prepare health-care product or medicine combination
for controlling appetite or pain sensation in mammals
DERWENT CLASS: B04; B07; D16
INVENTOR: CHUA A O; GOODNOW R A; GUBLER U A; HILTON H; JIN M; MARK
D F; MARTIN M L; PENG Y; ROSINSKI J A; ZHAO G; ZHOU X;
ZOU H; CHUA A; GOODNOW R; GUBLER U; MARK D; MARTIN M;
ROSINSKI J
PATENT ASSIGNEE: (HOFF-C) HOFFMANN LA ROCHE & CO AG F; (SHAN-N) SHANGHAI
INST BIOLOGICAL SCI CHINESE ACA; (SHAN-N) SHANGHAI LIFE
SCI INST CHINESE ACAD SCI
COUNTRY COUNT: 112

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2006111103	A1	20061026	(200682)*	ZH	31[5]	
CN 1850269	A	20061025	(200714)	ZH		
EP 1880730	A1	20080123	(200812)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2006111103	A1	WO 2006-CN772	20060424
CN 1850269	A	CN 2005-10025323	20050422
EP 1880730	A1	EP 2006-722399	20060424
EP 1880730	A1	WO 2006-CN772	20060424

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1880730	A1 Based on	WO 2006111103 A

PRIORITY APPLN. INFO: CN 2005-10025323 20050422
AN 2006-814717 [82] WPIDS
AB WO 2006111103 A1 UPAB: 20061222
NOVELTY - Use of mammalian ***GPR39*** protein or its modulator to
prepare health-care product or medicine combination for controlling

appetite or pain sensation of mammals, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:
(1) a health-care product or medicine combination for controlling appetite or pain sensation, containing the mammalian ***GPR39*** protein and a carrier; and
(2) identifying inhibitors of ***GPR39*** expression useful for reducing appetite or pain sensation, comprising inserting ***GPR39*** cDNA into an expression vector, transfecting mammalian cells with the vector, contacting the cells with test compounds, and measuring ***GPR39*** protein expression.
ACTIVITY - Analgesic; Anorectic.
No biological data given.
MECHANISM OF ACTION - ***GPR39*** modulator.
USE - The mammalian ***GPR39*** protein or its modulator is useful for preparing health-care product or medicine combination for controlling appetite or pain sensation of mammals (claimed).

L6 ANSWER 15 OF 22 WPIDS COPYRIGHT 2008 THE THOMSON CORP on STN
DUPLICATE 7

ACCESSION NUMBER: 2006-414788 [42] WPIDS
DOC. NO. CPI: C2006-130851 [42]
DOC. NO. NON-CPI: N2006-343464 [42]
TITLE: Identifying compounds for modulating gastrointestinal kinetics and/or cholesterol metabolism, comprises using G-protein coupled receptor 39 protein
DERWENT CLASS: B04; D16; J04; S03
INVENTOR: COULIE B; DEPOORTERE I; DEPOORTERE I I T; MOECHARS D; MOECHARS D W E; MOREAUX B; MOREAUX B C J; PEETERS T; PEETERS T L; PEETERS T L H; BENOITCHRISTIAN J M; DIEDERIK W E M; INGE I T D; THEOPHIEL L H P
PATENT ASSIGNEE: (JANC-C) JANSSEN PHARM NV
COUNTRY COUNT: 112

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2006058889	A1	20060608	(200642)*	EN	76[5]	
EP 1820026	A1	20070822	(200757)	EN		
NO 2007003294	A	20070829	(200765)	NO		
AU 2005311321	A1	20060608	(200780)	EN		
IN 2007DN04095	P1	20070824	(200780)	EN		
KR 2007086003	A	20070827	(200807)	KO		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

WO 2006058889 A1	WO 2005-EP56350 20051130
AU 2005311321 A1	AU 2005-311321 20051130
EP 1820026 A1	EP 2005-817427 20051130
EP 1820026 A1	WO 2005-EP56350 20051130
NO 2007003294 A	WO 2005-EP56350 20051130
IN 2007DN04095 P1	WO 2005-EP56350 20051130
IN 2007DN04095 P1	IN 2007-DN4095 20070530
NO 2007003294 A	NO 2007-3294 20070628
KR 2007086003 A	WO 2005-EP56350 20051130
KR 2007086003 A	KR 2007-713092 20070611

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1820026	A1	Based on	WO 2006058889	A
AU 2005311321	A1	Based on	WO 2006058889	A
KR 2007086003	A	Based on	WO 2006058889	A

PRIORITY APPLN. INFO: EP 2004-106220 20041201
AN 2006-414788 [42] WPIDS
AB WO 2006058889 A1 UPAB: 20060703
NOVELTY - Identifying compounds that modulate gastrointestinal kinetics and/or cholesterol metabolism comprises using all or part of the G-protein coupled receptor (GPR)39 protein.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) an isolated nucleic acid sequence selected from:
(i) a nucleic acid sequence encoding all or part of the polypeptides of SEQ ID NOS: 2 or 4, not given in the specification;
(ii) a nucleic acid sequence of SEQ ID NOS: 1 or 3, not given in the specification; or
(iii) a nucleic acid sequence having at least 80% sequence identity to the nucleic acid sequence of SEQ ID NOS: 1 or 3;
(2) a vector comprising a nucleic acid sequence;
(3) a host cell comprising a nucleic acid sequence or a vector; and
(4) a pharmaceutical composition, for the treatment of delayed gastric emptying and delayed colonic motility in a human or animal, comprising a ***GPR39*** receptor ***antagonist*** , or a pharmaceutical composition, for the treatment of increased gastric emptying and increased colonic motility in a human or animal, comprising a ***GPR39*** ***agonist*** , or a pharmaceutical composition, for the treatment of increased cholesterol levels in a human or animal, comprising a ***GPR39*** receptor ***agonist*** .
ACTIVITY - Gastrointestinal-Gen.; Anorectic; Antidiabetic; Cardiovascular-Gen; Antiarteriosclerotic; Metabolic. No biological data given.
MECHANISM OF ACTION - ***GPR39*** receptor ***antagonist***

; ***GPR39*** ***agonist*** .
USE - ***GPR39*** is used to identify compounds that modulate
gastrointestinal kinetics and/or cholesterol metabolism. A ***GPR39***
antagonist is useful in manufacturing a medicament for the
treatment of a disease condition related to delayed gastric emptying and
delayed colonic motility. The ***GPR39*** ***agonist*** is useful
in manufacturing a medicament for the treatment of a disease condition
related to increased gastric emptying, increased colonic motility, or
increased cholesterol levels (all claimed). The method is useful for
identifying compounds that modulate gastrointestinal kinetics and/or
cholesterol. The compounds, compositions, and methods are useful for
treating a disease, e.g. obesity, diabetes, or cardiovascular diseases
such as atherosclerosis.

L6 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1097408 CAPLUS <<LOGINID::20080428>>
DOCUMENT NUMBER: 145:433261
TITLE: Human marker genes and agents for diagnosis, treatment
and prophylaxis of cardiovascular disorders and atherosclerosis
INVENTOR(S): Betz, Ulrich; D'Urso, Donatella; Kolkhof, Peter;
Seewald, Michael; Strayle, Jochen; Grabner, Anne;
Hannus, Michael
PATENT ASSIGNEE(S): Bayer Healthcare A.-G., Germany
SOURCE: PCT Int. Appl., 84pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006108581	A2	20061019	WO 2006-EP3216	20060408
WO 2006108581	A3	20070412		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD,

SE,
SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,
VC,
VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU,
IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF,
BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW,
GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY,
KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
PRIORITY APPLN. INFO.: US 2005-671832P P
20050415
AB The invention relates to novel targets in the screening for compds.
useful
in the treatment and/or prophylaxis of a disease selected from the
group
comprising cardiovascular diseases, disorders of lipid metab. or
atherosclerosis. A human druggable genome siRNA library was
screened in a
cellular assay based on expression of LDL receptor as measured by
binding
of LDL-DiI in Huh7 hepatoma cells. Screening data and gene-
specific
information is provided for 467 siRNAs targeting 467 different
genes,
selected as positives from the total no. of screened genes. The
invention
relates to novel compds. for use as a medicament for diseases or
conditions involving a disease selected from the group comprising
cardiovascular diseases, disorders of lipid metab., or
atherosclerosis.
The invention esp. relates to ***antagonists*** and
expression-inhibitory compds. that target G-protein coupled
receptors
(GPCRs), kinases, and proteases. The invention further relates to
methods
for identifying these ***antagonists*** and expression-
inhibitory
compds., and methods for diagnosing the selected diseases.

L6 ANSWER 17 OF 22 WPIDS COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-284988 [29] WPIDS
DOC. NO. CPI: C2005-088413 [29]
DOC. NO. NON-CPI: N2005-233785 [29]
TITLE: Screening substance having e.g. apoptosis
induction
activity by contacting test substance and cell
expressing
G protein coupled receptors (approximately 75)
e.g. GPR91
and CD97, and detecting effect of substance on
receptor
DERWENT CLASS: B04; D16; S03
INVENTOR: KASHIWAKURA J; KAWAI H; MIURA K; OBAYASHI M;
OKAYAMA Y;
SAITO H; SASAKI K; YOSHIDA T
PATENT ASSIGNEE: (KYOW-C) KYOWA HAKKO KOGYO KK; (RIKE-C) RIKEN KK

COUNTRY COUNT: 106

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005028667	A1	20050331	(200529)*	JA	82[0]	
JP 2005514139	X	20061130	(200681)	JA	81	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005028667	A1	WO 2004-JP14136	20040921
JP 2005514139	X	WO 2004-JP14136	20040921
JP 2005514139	X	JP 2005-514139	20040921

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
JP 2005514139	X	Based on	WO 2005028667	A

PRIORITY APPLN. INFO: JP 2003-328980 20030919
AN 2005-284988 [29] WPIDS
AB WO 2005028667 A1 UPAB: 20051222
NOVELTY - Screening substance having apoptosis induction, human mast cell activation inhibition, degranulation suppression, suppression of production of inflammatory mediator, suppression of cytokine production or suppression of chemokine production activity, by contacting test substance and cell expressing G protein coupled receptor (GPCR) chosen from approximately 75 receptors e.g. GPR91, GPR105 and CD97, and detecting effect of substance on receptor.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) screening (M1b) a substance capable of controlling the glucocorticoid activity, involves contacting a test substance and a cell or a membrane fraction containing the cell expressing a receptor (R2) preferably GPCR expressed on human mast cells the expression level of which is modulated by the stimulation of glucocorticoid and chosen from complement component 3 receptor 1 (C3aR1), GPR34, beta2 adrenoreceptor (beta2), GPR105, TM7SF, fMLP1, P2Y8, A3, CRTH2, CCRL2, P2Y5, A2a, Epstein-Barr virus inducting gene 2 (EBI2), thrombin receptor (PAR1), H4, GPCR RE2 (RE2), CALCRL and EP4, and detecting the effect of the test substance on the receptor;
(2) method for performing an activity chosen from A1, involves utilizing ***agonist*** , ***antagonist*** or functional modulator

of R1 or siRNA or antisense DNA specific to a gene which suppresses the
expression of R1;
(3) treating (M2) atopic dermatitis, asthma, chronic obstructive
pulmonary diseases (COPD) or allergic disease, involves utilizing
agonist , ***antagonist*** or functional modulator of R1 or
siRNA or antisense DNA specific to a gene which suppresses the expression
of R1;
(4) controlling glucocorticoid activity, involves utilizing
agonist , ***antagonist*** or functional modulator of R2 or
siRNA or antisense DNA specific to a gene which suppresses the expression
of R2;
(5) pharmaceutical (I) for performing any one of A1 or for atopic
dermatitis, asthma, COPD or allergic disease, comprising ***agonist***
, ***antagonist*** or functional modulator of R1 or siRNA or antisense
DNA specific to a gene which suppresses the expression of R1 as an active
ingredient;
(6) agent (II) for controlling glucocorticoid activity, comprising
agonist , ***antagonist*** or functional modulator of R2 or
siRNA or antisense DNA specific to a gene which suppresses the expression
of R2 as an active ingredient;
(7) use of ***agonist*** , ***antagonist*** or functional
modulator (III) of R1 for manufacturing a medicament for treating atopic
dermatitis, asthma, COPD or allergic disease;
(8) antibody (IV) capable of specifically reacting with R1 and
having an activity chosen form A1;
(9) antibody (V) capable of controlling the glucocorticoid activity
and specifically reacting with R2;
(10) pharmaceutical (Ia) for performing any one of A1 or for atopic
dermatitis, asthma, COPD or allergic disease, comprising (IV) as an active
ingredient; and
(11) agent (IIa) for controlling glucocorticoid activity, comprising (V) as an active ingredient.
ACTIVITY - Dermatological; Antiasthmatic; Respiratory-Gen.; Antiallergic.
MECHANISM OF ACTION - Antisense therapy; Modulation of R1 or R2;
Mast cell activation inhibitor.
No biological data given.
USE - (M1) is useful for screening substance having one or more
activity chosen from apoptosis induction, human mast cell

activation
inhibition, degranulation suppression, suppression of production of inflammatory mediator, suppression of cytokine production and suppression
of chemokine production. (M1b) is useful for screening a substance capable
of controlling the glucocorticoid activity. (M2), (I) or (Ia) is useful
for treating atopic dermatitis, asthma, chronic obstructive pulmonary
diseases (COPD) or allergic disease. (II) or (IIa) is useful for controlling glucocorticoid activity. (III) is useful for manufacturing a
medicament for treating atopic dermatitis asthma, COPD or allergic disease
(claimed).

L6 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1170516 CAPLUS <<LOGINID::20080428>>
DOCUMENT NUMBER: 143:432610
TITLE: Methods for screening ***antagonists*** and/or ***agonists*** of binding of G protein-coupled receptor ***GPR39*** and ligands involved in cholesterol metabolism
INVENTOR(S): Fujii, Ryo; Nishi, Kazunori; Tanaka, Yasuhiro; Mori, Masaaki
PATENT ASSIGNEE(S): Takeda Pharmaceutical Company Limited, Japan
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005103283	A1	20051103	WO 2005-JP8271	20050422

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,

EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG
EP 1743944 A1 20070117 EP 2005-736916 20050422
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR
US 20070117160 A1 20070524 US 2006-587285 20061019
PRIORITY APPLN. INFO.: JP 2004-128169 A 20040423
WO 2005-JP8271 W 20050422
AB Disclosed is a method for screening an ***agonist*** / ***antagonist*** , etc. In particular, there is provided, for example, a method of screening an ***agonist*** or ***antagonist*** characterized by use of a G-protein-conjugated receptor protein contg. an amino acid sequence identical with or substantially identical with the amino acid sequence of SEQ ID NO: 1 or a salt thereof together with a substance assocd. with cholesterol metab. so as to effect screening of an ***agonist*** or ***antagonist*** as for the above receptor protein or salt thereof. The ***agonists*** and/or ***antagonists*** are useful for diagnosis and treatment of diseases assocd. with alteration of binding of G protein-coupled receptor ***GPR39*** with cholesterol metab.-related substance or their signal transduction change. The ***agonists*** and ***antagonists*** include antibodies, polynucleotides, antisense polynucleotide and other compds. He disease includes inflammatory bowel disease, gastrointestinal motility disorder, allergic gastrointestinal symptom, encopresis, colitis, excessive immune response post-transplant, Crohn's disease and related vomiting.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 19 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:965483 CAPLUS <<LOGINID::20080428>>
DOCUMENT NUMBER: 141:388614
TITLE: Novel screening method
INVENTOR(S): Ito, Yasuaki; Fujii, Ryo; Kobayashi, Makoto; Hinuma, Shuji; Hashimoto, Tadatoshi; Tanaka, Yasuhiro
PATENT ASSIGNEE(S): Takeda Pharmaceutical Company Limited, Japan
SOURCE: PCT Int. Appl., 176 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004097411	A1	20041111	WO 2004-JP5947	20040423
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
JP 2004340957	A	20041202	JP 2004-128141	20040423
EP 1619499	A1	20060125	EP 2004-729276	20040423
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
US 20060216286	A1	20060928	US 2005-552014	20051012
PRIORITY APPLN. INFO.:			JP 2003-122464	A 20030425
			WO 2004-JP5947	W 20040423

AB By using a G protein-coupled receptor protein having an amino acid sequence which is the same or substantially the same as the amino acid sequence represented by SEQ ID NO:1 or its salt and an ion chem. available metal element or its salt, an ***agonist*** or an ***antagonist*** to the above receptor protein or its salt can be efficiently screened.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 20 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:371064 CAPLUS <<LOGINID::20080428>>
DOCUMENT NUMBER: 140:373461
TITLE: Evaluation of breast cancer states and outcomes using
gene expression profiles
INVENTOR(S): West, Mike; Nevins, Joseph R.; Huang, Andrew
PATENT ASSIGNEE(S): Synpac, Inc., USA; Duke University
SOURCE: PCT Int. Appl., 799 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004037996	A2	20040506	WO 2003-US33656	20031024
WO 2004037996	A3	20041229		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20040083084	A1	20040429	US 2002-291878	20021112
WO 2004044839	A2	20040527	WO 2002-US38216	20021112
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,				

CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 20040106113 A1 20040603 US 2002-291886
20021112
AU 2003284880 A1 20040513 AU 2003-284880
20031024
PRIORITY APPLN. INFO.: US 2002-420729P P
20021024
US 2002-421062P P
20021025
US 2002-421102P P
20021025
US 2002-424701P P
20021108
US 2002-424715P P
20021108
US 2002-424718P P
20021108
US 2002-291878 A
20021112
US 2002-291886 A
20021112
US 2002-425256P P
20021112
WO 2002-US38216 A
20021112
WO 2002-US38222 A
20021112
US 2003-448461P P
20030221
US 2003-448462P P
20030221
US 2003-457877P P
20030327
US 2003-458373P P
20030331
WO 2003-US33656 W
20031024
AB The present invention relates generally to a method for evaluating and/or predicting breast cancer states and outcomes by measuring gene and metagene expression levels and integrating such data with clin. risk factors. Genes and metagenes whose expressions are correlated with a particular breast cancer risk factor or phenotype are provided using binary prediction tree modeling. The invention provides 175 genes assocd. with metagene predictors of lymph node metastasis, 216 genes assocd. with metagene predictors of breast cancer recurrence, and 496 metagenes related to breast cancer study. Methods of using the subject genes and metagenes in diagnosis and treatment methods, as well as drug screening methods, etc are also provided. In addn., reagents, media and kits that find use in practicing the subject methods are also provided.

L6 ANSWER 21 OF 22 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2004643243 MEDLINE <<LOGINID::20080428>>
DOCUMENT NUMBER: PubMed ID: 15383539
TITLE: Common structural basis for constitutive activity of the
ghrelin receptor family.
AUTHOR: Holst Birgitte; Holliday Nicholas D; Bach Anders; Elling
Christian E; Cox Helen M; Schwartz Thue W
CORPORATE SOURCE: Laboratory for Molecular Pharmacology, Department of
Pharmacology, The Panum Institute, University of
Copenhagen, Blegdamsvej 3, DK-2200, Copenhagen,
Denmark..
b.holst@molpharm.dk
SOURCE: The Journal of biological chemistry, (2004 Dec 17) Vol.
279, No. 51, pp. 53806-17. Electronic Publication:
2004-09-21.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 29 Dec 2004
Last Updated on STN: 5 Feb 2005
Entered Medline: 4 Feb 2005

AB Three members of the ghrelin receptor family were characterized in parallel: the ghrelin receptor, the neurotensin receptor 2 and the orphan receptor ***GPR39*** . In transiently transfected COS-7 and human embryonic kidney 293 cells, all three receptors displayed a high degree of ligand-independent signaling activity. The structurally homologous motilin receptor served as a constitutively silent control; upon ***agonist*** stimulation, however, it signaled with a similar efficacy to the three related receptors. The constitutive activity of the ghrelin receptor and of neurotensin receptor 2 through the G(q), phospholipase C pathway was approximately 50% of their maximal capacity as determined through inositol phosphate accumulation. These two receptors also showed very high constitutive activity in activation of cAMP response element-driven transcription. ***GPR39*** displayed a clear but lower degree of constitutive activity through the inositol phosphate and cAMP response element pathways. In contrast, ***GPR39*** signaled with the highest constitutive activity in respect of activation of serum response element-dependent transcription, in part, possibly, through G (12/13) and Rho kinase. Antibody feeding experiments demonstrated that the epitope-tagged ghrelin receptor was constitutively internalized but

could
be trapped at the cell surface by an inverse ***agonist*** , whereas
GPR39 remained at the cell surface. Mutational analysis showed
that the constitutive activity of both the ghrelin receptor and
GPR39 could systematically be tuned up and down depending on the
size and hydrophobicity of the side chain in position VI:16 in the context
of an aromatic residue at VII:09 and a large hydrophobic residue at
VII:06. It is concluded that the three ghrelin-like receptors display an
unusually high degree of constitutive activity, the structural basis for
which is determined by an aromatic cluster on the inner face of the
extracellular ends of TMs VI and VII.

L6 ANSWER 22 OF 22 WPIDS COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-282100 [29] WPIDS
DOC. NO. CPI: C2001-086033 [29]
DOC. NO. NON-CPI: N2001-201041 [29]
TITLE: Predicting mutants that alter the activity of receptors
using multiple sequence alignment and phylogenetic profiling, useful e.g. for altering the activities of
orphan proteins
DERWENT CLASS: B04; D16; S03
INVENTOR: PACKER J C; WENHAM D
PATENT ASSIGNEE: (BIOF-N) BIOFOCUS DISCOVERY LTD; (CAMB-N) CAMBRIDGE DRUG
DISCOVERY LTD; (WILL-I) WILLIAMS K M
COUNTRY COUNT: 89

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2001027632	A2	20010419	(200129)*	EN	89[10]	
AU 2000076780	A	20010423	(200147)	EN		
AU 2000276780	A8	20050908	(200568)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001027632	A2	WO 2000-IB1407	20001002
AU 2000076780	A	AU 2000-76780	20001002
AU 2000276780	A8	AU 2000-276780	20001002
AU 2000076780	A	WO 2000-IB1407	20001002
AU 2000276780	A8	WO 2000-IB1407	20001002

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000076780	A	Based on	WO 2001027632 A
AU 2000276780	A8	Based on	WO 2001027632 A

PRIORITY APPLN. INFO: WO 2000-IB1407 20001002
AN 2001-282100 [29] WPIDS
AB WO 2001027632 A2 UPAB: 20060117
NOVELTY - Methods of predicting mutations (mut.s) that alter the activity
of a receptor (rec.) in a desired manner, comp. utilizing multiple sequence alignment and phylogenetic profiling to identify the relatives of
a given rec. that are most likely to provide useful data allowing prediction of sites to mutate in the given rec., are new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the
following:
(1) a method (I) of predicting a site for mut. of a first cellular
rec. (CR) (CR1) (the mut. alters the activity of CR1), comp.:
(a) performing a multiple sequence alignment of CR1 with other CRs
in the same rec. family;
(b) allocating CR1 to a rec. sub-family; and
(c) selecting an amino acid (aa) residue of CR1 for mut. (the aa
residue is analogous to a residue of a second rec., the mut. of which is
known to cause altered activity of a second CR (CR2), this is predictive
of a site for mut. in CR1);
(2) a method (II) of obtaining a mutant of a CR1 (the mutant has
altered activity as compared to the WT CR1), comp.:
(i) steps (a) - (c) from (I);
(ii) mutating the selected aa residue of the CR; and
(iii) expressing the mut'd CR in a cell;
(3) a mutated (mut'd) GPR8 rec. comprising (comp.) altered activity
as compared to a wild type (WT) GPR8 rec. (the GPR8 rec. comprises a mut.
selected from a mut. at aa 124 from Asp to Ala, a mut. at aa 127 from Asp
to Ala and/or a mut. at aa 259 from Thr to Glu);
(4) a mut'd GPR7 rec. comp. altered activity as compared to a WT
GPR7 rec. (the GPR7 rec. comprises a mut. selected from a mut. at aa 116
from Asp to Ala, a mut. at aa 119 from Asn to Ala and/or a mut. at aa 250
from Thr to Glu);
(5) a mut'd GPR10 rec. comp. altered activity as compared to a WT
GPR10 rec. (the GPR10 rec. comprises a mut. selected from a mut. at aa 224
from Tyr to Glu, and/or a mut. at aa 247 from Val to Glu);
(6) a mut'd GPR17 rec. comp. altered activity as compared to a WT
GPR17 rec. (the GPR17 rec. comprises a mut. selected from a mut. at aa 114
from Asn to Ala and/or a mut. at aa 234 from Val to Glu);
(7) a mut'd GPR4 rec. comp. altered activity as compared to a WT
GPR4 rec. (the GPR4 rec. comprises a mut. selected from a mut. at

aa 100
from Asn to Ala and/or a mut. at aa 223 from Lys to Glu);
(8) a mut'd GPR15 rec. comp. altered activity as compared to
a WT
GPR15 rec. (the GPR15 rec. comprises a mut. selected from a mut. at
aa 116
from Asn to Ala and/or a mut. at aa 240 from Ile to Glu);
(9) a mut'd GPR20 rec. comp. altered activity as compared to
a WT
GPR20 rec. (the GPR20 rec. comprises a mut. selected from a mut. at
aa 133
from Asn to Ala and/or a mut. at aa 230 from Ile to Glu);
(10) a mut'd EB12 rec. comp. altered activity as compared to
a WT
EB12 rec. (the EB12 rec. comprises a mut. selected from a mut. at
aa 114
from Asn to Ala and/or a mut. at aa 243 from Leu to Glu);
(11) a mut'd BONZO rec. comp. altered activity as compared
to a WT
BONZO rec. (the BONZO rec. comprises a mut. selected from a mut. at
aa 112
from Asn to Ala and/or a mut. at aa 230 from Leu to Glu);
(12) a mut'd RDC1 rec. comp. altered activity as compared to
a WT
RDC1 rec. (the RDC1 rec. comprises a mut. selected from a mut. at
aa 127
from Asn to Ala and/or a mut. at aa 259 from Thr to Glu);
(13) a mut'd O15218 rec. comp. altered activity as compared
to a WT
O15218 rec. (the O15218 rec. comprises a mut. selected from a mut.
at aa
136 from Asn to Ala and/or a mut. at aa 257 from Cys to Glu);
(14) a mut'd H963 rec. comp. altered activity as compared to
a WT
H963 rec. (the H963 rec. comprises a mut. selected from a mut. at
aa 97
from Asn to Ala and/or a mut. at aa 222 from Leu to Glu);
(15) a mut'd GPR30 rec. comp. altered activity as compared
to a WT
GPR30 rec. (the GPR30 rec. comprises a mut. selected from a mut. at
aa 140
from Asn to Ala and/or a mut. at aa 258 from Leu to Glu);
(16) a mut'd GPR2 rec. comp. altered activity as compared to
a WT
GPR2 rec. (the GPR2 rec. comprises a mut. selected from a mut. at
aa 238
from Leu to Glu);
(17) a mut'd GPR5 rec. comp. altered activity as compared to
a WT
GPR5 rec. (the GPR5 rec. comprises a mut. selected from a mut. at
aa 224
from Val to Glu);
(18) a mut'd GPR13 rec. comp. altered activity as compared
to a WT
GPR13 rec. (the GPR13 rec. comprises a mut. selected from a mut. at
aa 230
from Ile to Glu);
(19) a mut'd GPR18 rec. comp. altered activity as compared
to a WT
GPR18 rec. (the GPR18 rec. comprises a mut. selected from a mut. at

aa 231
from Ile to Glu);
(20) a mut'd GPR21 rec. comp. altered activity as compared to a WT
GPR21 rec. (the GPR21 rec. comprises a mut. selected from a mut. at aa 251
from Ala to Glu);
(21) a mut'd GPR22 rec. comp. altered activity as compared to a WT
GPR22 rec. (the GPR22 rec. comprises a mut. selected from a mut. at aa 312
from phenylAla to Glu);
(22) a mut'd GPR25 rec. comp. altered activity as compared to a WT
GPR25 rec. (the GPR25 rec. comprises a mut. selected from a mut. at aa 230
from Leu to Glu);
(23) a mut'd GPR31 rec. comp. altered activity as compared to a WT
GPR31 rec. (the GPR31 rec. comprises a mut. selected from a mut. at aa 221
from glutamine to Glu);
(24) a mut'd GPR38 rec. comp. altered activity as compared to a WT
GPR38 rec. (the GPR38 rec. comprises a mut. selected from a mut. at aa 297
from Val to Glu);
(25) a mut'd ***GPR39*** rec. comp. altered activity as compared to a WT ***GPR39*** rec. (the ***GPR39*** rec. comprises
a mut. selected from a mut. at aa 282 from Ile to Glu);
(26) a mut'd GPR40 rec. comp. altered activity as compared to a WT
GPR40 rec. (the GPR40 rec. comprises a mut. selected from a mut. at aa 223
from Ala to Glu);
(27) a mut'd GPR41 rec. comp. altered activity as compared to a WT
GPR41 rec. (the GPR41 rec. comprises a mut. selected from a mut. at aa 224
from Ala to Glu);
(28) a mut'd GPR42 rec. comp. altered activity as compared to a WT
GPR42 rec. (the GPR42 rec. comprises a mut. selected from a mut. at aa 224
from Ala to Glu);
(29) a mut'd GPR43 rec. comp. altered activity as compared to a WT
GPR43 rec. (the GPR43 rec. comprises a mut. selected from a mut. at aa 221
from Val to Glu);
(30) a mut'd MGR rec. comp. altered activity as compared to a WT
MGR rec. (the MGR rec. comprises a mut. selected from a mut. at aa 263
from Tyr to Glu); and
(31) a method (III) of identifying a compound that modulates the
activity of the rec.s above, comp.:
(A) contacting a candidate compound with the rec.; and

(B) determining the activity of the rec. in the presence of the compound (a difference in rec. activity in the presence and absence of the candidate compound is indicative of compound modulation).

USE - The methods are applicable to any type of rec., and are particularly well suited for predicting sites to mutate in order to alter the activities of orphan rec.s for which no ***agonists*** are known.

In particular, the method is used to predict cellular rec. mut.s that induce the rec. to constitutively activate it's downstream signaling activities.

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